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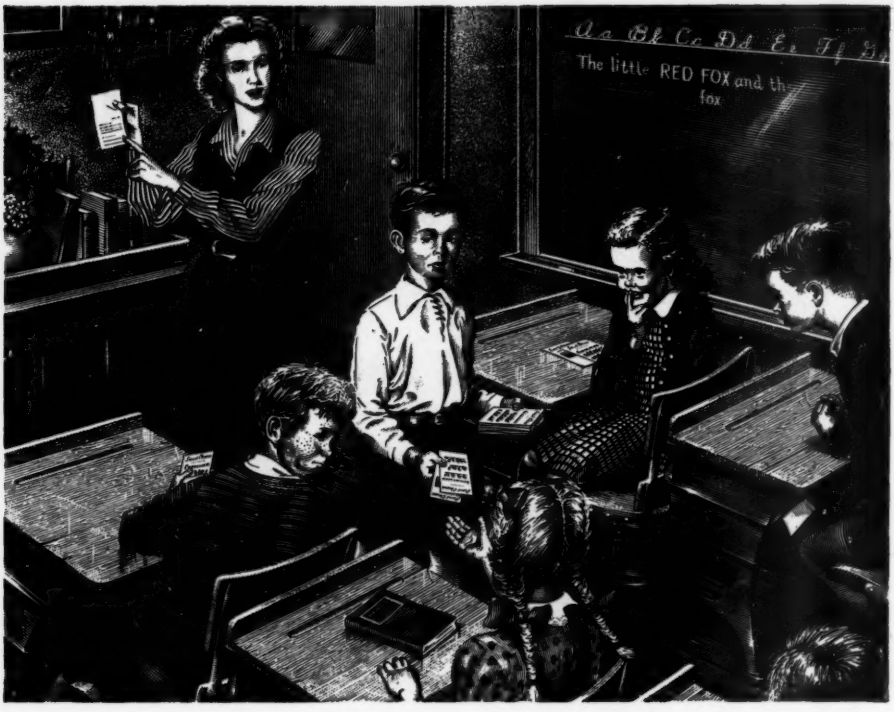

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AMERICAN JOURNAL OF PHARMACY

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CONTENTS

E D I T O R I A L

TINCTURE OF IODINE.

THE change in the strength of Iodine Tincture with the advent of the U. S. P. XIII has caused no little confusion amongst pharmacists. Some clarification of the issue may be in order.

Research over ten years ago proved that 2 per cent iodine was sufficiently active as a bactericide for general use as a germicide. The 7 per cent tincture was shown to be not only stronger than necessary, but also irritating due to its high iodine, iodide and alcohol content. An ideal product was proposed containing 2 per cent iodine and 2.4 per cent sodium iodide in distilled water. Such a product being practically isotonic with tissue fluids is non-irritating. The use of sodium iodide in place of potassium iodide was based upon its lesser toxicity to tissue. The U. S. P. XII recognized this as *Solution of Iodine*. A similar product was recognized in the U. S. P. XII as *Mild Tincture of Iodine*. This differed only in the use of diluted alcohol as the solvent rather than distilled water. This Mild Tincture of Iodine was preferred over Iodine Solution by many users, since it dried more rapidly and it did not freeze at low temperatures. The low freezing point made it more suitable for first aid kits and use in cold regions.

Experience with this Mild Tincture of Iodine was so satisfactory that the Pharmacopoeial Revision Committee decided to delete the 7 per cent tincture entirely and to give its title, Iodine Tincture, to that product formerly known as Mild Tincture of Iodine. To make things more complicated the N. F. Committee placed the 7 per cent tincture in the N. F. VIII as *Strong Iodine Tincture* and deleted its long recognized *Stronger Tincture of Iodine* now unofficial. There are then today the following Iodine Tinctures official:

Iodine Tincture U. S. P. XIII,
2% iodine, 2.4% sodium iodide in diluted alcohol.

Strong Iodine Tincture N. F. VIII,
7% iodine, 5% potassium iodide, alcohol content 83-88% by volume.

Many pharmacists have failed to appreciate their professional responsibilities in selling these products. Many customers now asking for Tincture of Iodine get the 7 per cent product. From the legal standpoint this is wrong unless the customer specifically asks for Tincture of Iodine *U. S. P. XII.* From the ethical standpoint it is the pharmacist's duty to explain to a customer wanting Iodine Tincture that the medical profession has approved its reduction in strength, since the older product was excessively strong and irritating when used as an antiseptic. If the product is to be used as a counter-irritant, which is sometimes the case, the Strong Iodine Tincture should be recommended, since it is to be used on the unbroken skin. The Strong Tincture is also quite useful in allaying itching in poison ivy dermatitis.

The tragedy of this general confusion lies in the realization that many pharmacists have failed to measure up to their oft-repeated statement that "the pharmacist is more than a merchant." Here is a specific instance of where a really professional man would take the time to translate a medical advance involving a home remedy to his customer, even though the sale amounted to only twenty-five cents. This is our public duty as pharmacists. How many times have we argued that the pharmacist is the only one sufficiently informed and conscious of public welfare to sell drugs? Yet many pharmacists have given no attention at all to the sale of this commodity, which sale we do not believe others competent to handle. It is high time that many retail pharmacists appreciate the fact that our special privileges in the sale of drugs involves special responsibilities and to have these privileges is possible only so long as we discharge our public duties in a satisfactory manner.

Manufacturers and wholesalers, in some instances, have also failed in their service to pharmacists in that they have not supplied the new tincture without delay. Some still ship the 7 per cent tincture when iodine tincture is ordered, labelling it U. S. P. XII, or Strong Iodine Tincture N. F. This does not violate any law, but it does deny the pharmacist what he has requested and makes it difficult for him to sell the proper product. The average pharmacist cannot make Iodine Tincture economically, for he has only tax-paid alcohol. The manufacturer uses a specially denatured, tax-free alcohol, since it is for a non-beverage product. The pharmacist, therefore, hesitates to make the product himself because of the cost in-

volved. All in all we have not established a very enviable record in our handling of the iodine situation.

In summary, let us hope that all pharmacists will appreciate more fully their obligation in translating all medical and pharmaceutical advances into actual practice for the public welfare. This is our plain duty and it cannot be transferred to others without at the same time surrendering our cherished prerogatives as pharmacists.

L. F. Tice.

EXPERIMENTS IN THE DEVELOPMENT OF A LOTION HAVING AN ACID PH

By Kenneth E. Avis, M. Sc.*

THE "baby lotion" developed by Clarke and Flack(1) for inclusion in the New York Hospital Formulary made use of a triethanolamine soap as the emulsifying agent. Clinical trial showed the formula to be non-irritant to the skin of new-born infants although the pH was approximately 8.5. This product was developed because it was felt that an emulsion would effectively cleanse the new-born infant's skin by removing both water-soluble and oil-soluble debris and would also provide the emollient value of an oil. In addition, it was evident that an emulsion would be much more pleasant than an oil for the nurse or mother to apply.

Research Objective

Although the clinical trial showed that this preparation was non-irritant to the tender skin of the new-born infant it has been suggested that a pH so high on the alkaline side should be much less desirable than a pH nearer to that of the normal skin. Also, the entirely non-irritant character of the new non-ionic surface active agents suggested the use of one of these compounds as the emulsifying agent in a dermatologic lotion. With these suggestions in mind an attempt was made to prepare a stable emulsion having a pH slightly on the acid side using a non-ionic surface active substance as the emulsifying agent. No report of a stable acid emulsion has been found in pharmaceutical literature to this date. Therefore, it was felt that if such an emulsion could be developed, applications to pharmaceutical formulations other than baby lotions would be a probability.

Stability Tests

A basis for comparison of the stability of the products formulated in the following experimental work was a primary necessity. Such a basis was established: the effects resulting from a sample of the product standing undisturbed on a shelf at room temperature

* Lederle Graduate Research Fellow, Philadelphia College of Pharmacy and Science, Philadelphia, Pa. In partial fulfillment of the requirements for the degree of M. Sc. in Pharmacy. This research was supported by Lederle Laboratories Division, American Cyanamid Co.

for at least one month. All products were tested and compared in this way. However, in order to speed the determination of the stability of those preparations showing the most promise, two methods were used for accelerating creaming and determining stability. One method was the accepted procedure of placing a sample of the product in an oven at a temperature of 50° C. for a period of one week. A second method was that of placing a sample in a centrifuge. The sample was then spun at fifteen minute intervals for a total of two and one-half hours at approximately 1700 RPM or for a total of one and one-half hours at approximately 2000 RPM. The results from these three procedures for testing stability were found to be reasonably comparable when a final comparison was made among those preparations with which all three methods were employed.

The term "stability" as used in this paper has reference to the degree of creaming and the separation of oil from an emulsion. A stable emulsion was one which showed no evidence of creaming or separation of oil when tested by means of one or all of the three procedures described above.

General Procedure

In order to minimize variables as much as possible the following general procedure was used throughout this work for the compounding of formulæ. The oil phase was melted together and warmed to a temperature of about 60° C. The aqueous phase was warmed to a temperature of about 65° C. and then the oil phase was added slowly to the aqueous phase with constant stirring. This mixture was then passed through a hand homogenizer six times. The emulsifying agent and emulsification assistants in each case were incorporated in either the oil or the aqueous phase, depending with which they were miscible. It was found not to be necessary to control the mixing temperature of the oil and the aqueous phases within the limits of ± 5° C. of the temperatures previously specified.

Basic Oil Phase

During all of the experimental work the oil portion of the emulsions was essentially that of the Clarke and Flack formula, namely:

Lanolin, Anhydrous U. S. P.	6.4%
Liquid Petrolatum (heavy)	8.8%
Sesame Oil N. F.	1.1%
Corn Oil	1.1%

Because olive oil was unavailable, corn oil was used as a substitute. The reason for the fractional parts of the oils was not known, but in order to have a preparation with which to compare the results obtained the proportions used in the original Clarke and Flack formula were maintained.

Experimental

With Span 80 and Tween 60[1]

The first of the non-ionic surface active agents that were used in this work were Span 80 (sorbitan monooleate) and Tween 60 (sorbitan monolaurate polyoxyalkylene derivative). The concentrations of Span 80 ranged from 0.5 per cent to 4.0 per cent and that of Tween 60 from 1.0 per cent to 2.5 per cent. The concentration which seemed to produce the best results was a mixture of Span 80 2.0 per cent and Tween 60 1.0 per cent, although concentrations of Span 80 equal to or greater than that of Tween 60 within the range given above resulted in no pronounced difference in the stability of the products. In conjunction with these agents Cellosize WS 100[2] (hydroxy ethyl cellulose) in a concentration of 2.0 per cent or Cellosize WS 500 in a concentration of 1.0 per cent decreased the creaming rate and improved the stability of the emulsion more than any subsequent emulsification assistants used. Pharmagel A and Pharmagel B both either curded the emulsion or caused oil separation immediately or within a few days when used in concentration of 0.1 per cent to 2.0 per cent. Arlex[1] (commercial sorbitol) 1.0 per cent to 10.0 per cent improved the stability of the emulsion over the use of Span 80 and Tween 60 combinations alone, in that the rate of creaming was slowed and the degree of oil separation after standing for about a month was decreased. A 2 per cent solution of methyl cellulose (400 cps.) in concentrations from 0.2 per cent to 10.0 per cent seemed to accelerate the initial creaming but the degree of creaming and the amount of oil separation after standing for a month was reduced. When used as emulsification assistants Aerosol NS-8[3] (N-octaglycoxyethyl stearamide) and Aerosol NC-9[3] (N-nonaglycoxyethyl myristyl acid amides) did not materially alter the stability of the emulsion.

1. Donated by Atlas Powder Company, Wilmington, Del.

2. Donated by Carbide and Carbon Chemicals Corporation, 30 East 42nd St., New York 17, N. Y.

3. Experimental samples obtained from American Cyanamid Company, 30 Rockefeller Plaza, New York 20, N. Y.

The emulsions prepared with the use of Span 80 and Tween 60 in conjunction with the emulsification assistants Arlex, Cellosize WS 100, Cellosize WS 500, and methyl cellulose (2 per cent. solution of 400 cps.) appeared to be very smooth preparations when first made. Even when creaming had occurred after 24 hours, or within a few days, vigorous shaking of the bottle re-established a smooth preparation. The ease with which this occurred was most pronounced when Cellosize WS 100 2.0 per cent or Cellosize WS 500 1.0 per cent was used as the assistant. Also, with these four assistants accelerated creaming tests and standing on the shelf for about a month revealed but a few small oil globules separated on top and a secondary creamed layer that was opaque but distinguishable from the upper creamed portion. Some of the least satisfactory preparations in this series showed an oil separation layer of as much as 8.0 per cent above a creamed layer that left the lower portion opalescent or translucent. The pH of selected samples approximated that desired, ranging from 5.45 to 5.6. However, none of the forty different emulsions in this series exhibited stability for a minimum period of one month.

With Aerosol NS-8 and Aerosol NC-9

Aerosol NS-8 and Aerosol NC-9 were two non-ionic surface active agents next tried in emulsion formulation. It was found that Aerosol NC-9 alone produced an emulsion stable for only a brief period of time, while Aerosol NS-8 produced one of more prolonged stability. However, the use of Aerosol NC-9 in conjunction with Aerosol NS-8 seemed to produce an emulsion with somewhat greater stability than either alone. Concentrations of Aerosol NS-8 varying from 0.2 per cent to 2.0 per cent and of Aerosol NC-9 over the same range were tried. The ratio having the greatest stability and the minimal creaming was Aerosol NS-8 0.2 per cent and Aerosol NC-9 0.2 per cent, although there was no great difference in stability attributable directly to different concentrations of the Aerosols within the ranges given above.

A number of emulsification assistants were used along with the Aerosols in order to attempt to decrease the rate of creaming and to prevent the separation of oil when the sample was undisturbed for a month or more. Glyceryl monostearate did not noticeably improve the preparation in strengths of 0.2 per cent, and with 1.0 per cent there was noticeable curding and a more rapid rate of creaming.

Both Pharmagel A and Pharmagel B were used as assistants. Percentages ranging from 0.1 to 2.0 were tried with Aerosol NS-8 alone and with combinations of Aerosol NS-8 and Aerosol NC-9. Emulsions made with Pharmagel B all creamed rapidly and showed oil separation upon standing on the shelf for a month or when the accelerated stability tests were applied, although lower concentrations creamed less rapidly. One particular formulation with both of the Aerosols 0.2 per cent and Pharmagel B 1.0 per cent creamed rapidly. After standing three days a creamed layer of about 42 per cent and a lower translucent layer had become light gels. Shaking redispersed the layers with the re-formation of a fluid preparation. Observation, after subsequent standing for about a month on the shelf at room temperature, revealed a preparation which had creamed but there was no separation of oil, and fluidity had been maintained. The omission of Aerosol NC-9 in the formula produced a similar product but one in which there was oil separation. These two were the best formulæ in the series involving Pharmagel B.

Pharmagel A emulsions exhibited creaming very similar to those made with Pharmagel B. One formulation containing Aerosol NS-8 2.0 per cent and Pharmagel A 1.0 per cent creamed rapidly at first. After standing for about ten days the preparation showed a creamed layer of about 58 per cent with a lower translucent layer. Both layers were light gels. Vigorous shaking caused the layers to redisperse with the formation of a fluid emulsion. This then showed no evidence of creaming or of oil separation after having had a shelf life of a month. The emulsion was also fluid and fairly smooth. However, an attempt to duplicate the procedure resulted in a preparation which creamed and separated a few oil globules.

Up to an age of about 20 days Cellosize WS 500, Cellosize WS 100, and Cellosize WS 20 in percentages of 1 and 2 increased the ease with which the creamed material could be redispersed with shaking. Within a month, however, there was a separation of oil globules on top of the creamed material, thus making impossible complete redispersion upon shaking.

Percentages of 0.2 to 2.0 of Carbowax 1540 [4] (a polyethylene glycol) did not materially improve the preparations, although the amount of oil which separated after a month was reduced to a few very small oil globules.

4. Experimental samples obtained from Carbide and Carbon Chemicals Corporation.

Cetyl alcohol 0.1 per cent to 2.0 per cent, stearic acid 0.1 per cent, mucilage of acacia 0.2 per cent to 4.0 per cent, and methyl cellulose (2 per cent solution of 400 cps.) 0.2 per cent to 10.0 per cent used as emulsification assistants did not improve the final emulsion. Ageing for one month resulted in creamed preparations with at least a few globules of oil separated on top of the creamed material.

Emulsions prepared with Arlex as the assistant were in general somewhat improved and a few were markedly improved. A combination of Aerosol NS-8 6 per cent and Arlex 10 per cent resulted in a preparation which redispersed readily with shaking after creaming had occurred a few days subsequent to being made. After standing undisturbed for a month this emulsion showed creaming but no oil separation, and thus was among the best formulæ of this series. Concentrations of 1.0 to 20.0 per cent of Arlex were employed. The higher percentages provided the greatest stabilization when coupled with a higher percentage of Aerosol NS-8 (1.0 per cent to 6.0 per cent). In an effort further to improve the preparations of this series, the best developed thus far in the study, a number of other ingredients were used along with the Arlex and Aerosol NS-8. Glycerin 2 per cent to 5 per cent, propylene glycol 2 per cent to 5 per cent, ethanol 2 per cent, and Aerosol OT Aqueous [5] (di-octyl sodium sulfosuccinate) 2 per cent to 10 per cent as the other ingredients did not produce any marked improvement in the final products. Creaming and the separation of oil globules occurred in all of the aged samples. One exception to the appearance of oil globules in the month-old sample occurred in a formula having Aerosol NS-8 1.0 per cent, and Aerosol OT 10.0 per cent Aqueous 2.0 per cent, Arlex 2.0 per cent, and ethanol 2.0 per cent, but the emulsion showed creaming. This particular emulsion was found to have a pH of 5.3.

Aerosol OT was used in conjunction with the Aerosol NS-8 because Young and Coons(2) have suggested that a non-ionic surface active agent was often found not to produce satisfactorily stable emulsions alone, but that the addition of a small percentage of a cationic or an anionic surface active agent would improve the stability. Since Aerosol OT is an example of an anionic agent it was tried along with the Aerosol NS-8. However, the combination did not show greater stability than the Aerosol NS-8 alone.

5. Experimental samples presented by American Cyanamid Company.

As an example of a cationic agent Ceepryn chloride (cetyl pyridinium chloride) in a 1:1,000 solution was employed. Ceepryn chloride 1:1,000 in percentages of 2 and 10 did not improve the emulsions. A number of the assistants formerly employed were used with this new combination in order to determine the effect that they would have on the stability, but none of the assistants materially improved the formula. In every sample after standing for a month there was a distinct creamed layer and at least a few small oil globules separated on top of the creamed material. Those assistants which were used were: glycerin 2 per cent and 6 per cent; propylene glycol 2 per cent and 6 per cent; ethanol 6 per cent; Arlex 2 per cent and 10 per cent; Cellosize WS 100 2 per cent; methyl cellulose (2 per cent solution of 400 cps.) 2 per cent, 5 per cent, and 20 per cent; and a 1 per cent solution of sodium alginate 5 per cent, 40 per cent, and 81 per cent. The pH of selected formulæ in this group was determined and found to range between 4.1 and 5.4. The thought that this combination of Aerosol NS-8 and Ceepryn chloride might be more stable in alkaline medium prompted the use of dilute ammonium hydroxide solution to bring the pH up to about 10. However, the resulting products in each of the instances tried were less stable than before the ammonium hydroxide solution was added. There was more curding of the creamed material and more separation of oil. When first prepared a number of the formulæ in this series of 135 involving Aerosol NS-8 and Aerosol NC-9 yielded products which seemed to be fine emulsions. Emulsification took place readily, at times with stirring alone before being passed through the hand homogenizer. The creaming which occurred during the first few days after preparation was very easily redispersed with a few shakes of the bottle. However, not one formula in the series proved to be satisfactory when aged for a month on a shelf at room temperature or tested by means of one of the two accelerated procedures used in this work.

With Emcol MS-16[6]

Another surface active agent used as an emulsifying agent in a series of forty formulæ was a blend of a non-ionic and a cationic substance. This agent, Emcol MS-16, was a blend of glyceryl monostearate and a quaternary ammonium compound [a derivative of a

6. Experimental samples supplied by The Emulsol Corporation, 59 East Madison St., Chicago 3, Ill.

fatty acid ester of 1-(2-hydroxyethylcarbamylmethyl) pyridinium chloride]. Literature from the manufacturer stated that it had been found that emulsions produced by a non-ionic substance alone were not stable but that the addition of a controlled amount of a cationic substance materially improved the stability of the emulsion produced. When using Emcol MS-16 it was found that an emulsion did not form readily with stirring but that homogenization in a hand homogenizer produced a smooth emulsion. The consistency of the product could be controlled by the percentage of Emcol MS-16 employed. A 1.0 per cent to 2.0 per cent concentration would produce a smooth fluid emulsion but a concentration of 10.0 per cent would yield an emulsion which was a light cream in consistency, with apparently good stability. Although the fluid emulsions formed with Emcol MS-16 exhibited less creaming than any of the previous ones prepared with other surface active agents, month-old samples showed noticeable creaming and also a small amount of oil separation. Consequently, a number of the emulsification assistants were combined with the emulsifying agent in order to attempt to improve the product. Even when the Emcol MS-16 was used in as little as 1.0 per cent and 2.0 per cent concentrations, the addition of Stenol [7] 1.0 per cent, Emcol MS [8] 1.0 per cent and 2.0 per cent, Arlex 4.0 per cent, cetyl alcohol 1.0 per cent, and glyceryl monostearate 1.0 per cent resulted in a somewhat curded and gellified preparation. A 1 per cent solution of sodium alginate produced marked curding and gelling immediately.

Cellosize WS 100, propylene glycol, glycerin, ethanol, and methyl cellulose (2 per cent solution of 400 cps.) all improved the preparations to some degree when used in percentages ranging from 1.0 to 20.0 along with Emcol MS-16 1.0 per cent and 2.0 per cent. The products from these combinations usually exhibited a creaming when centrifuged for one and one-half hours at 2,000 RPM but the lower layer maintained varying degrees of opacity. A small amount of oil separated in most cases upon centrifuging but the month-old shelf sample did not show any oil separation. Since these products still were not entirely satisfactory, combinations involving two of the assistants were made an object of experimentation. Methyl cellulose seemed to be slightly the best stabilizer of this group and so was

7. Experimental samples supplied by E. I. duPont de Nemours & Co., Wilmington 98, Del.

8. Experimental samples supplied by The Emulsol Corporation.

employed as one of the ingredients in each test formula. In order to avoid too much thickening effect from the assistants alone, the other ingredient used was either propylene glycol or ethanol. An improvement was evident when two assistants were employed in that the rate and degree of creaming became less. Stability tests indicated that the combination of Emcol MS-16, propylene glycol, and methyl cellulose was slightly superior to those in which ethanol replaced the propylene glycol. The proportions of methyl cellulose ranged from 10.0 per cent to 30.0 per cent and of ethanol and propylene glycol from 6.0 per cent to 12.0 per cent. From these last combinations the following formula was selected as being the most satisfactory, and as the acid emulsion formula of choice from all of the experimental preparations developed in this work:

Lanolin, Anhydrous U. S. P.	6.4%
Liquid Petrolatum (heavy)	8.8%
Sesame Oil N. F.	1.1%
Corn Oil	1.1%
Emcol MS-16	2.0%
Methyl Cellulose (400) 2%	20.0%
Propylene Glycol	20.0%
Water	40.6%

A sample of this formula centrifuged for one and one-half hours at 2,000 RPM at 15 minute intervals showed no evidence of creaming but there was present a thin somewhat tenacious film on the top. After this centrifuged sample stood undisturbed for four days the film on top had become more thickened but there was no free oil and no evidence of creaming. An identical sample was placed in an oven for one week at a temperature of 50° C. and then at room temperature for four days. This sample showed a creamed layer of about 30 per cent with a lower layer that was opaque with the exception of a narrow clearing zone at the very bottom. There was no oil separation. The same sample allowed to stand undisturbed for 23 additional days at room temperature showed a creamed layer of about 60 per cent which was quite thick. However, there was no oil separation and a few shakes of the bottle redispersed the creamed material easily to a smooth emulsion. In no other emulsion prepared had this been possible. A third identical sample which had been standing undisturbed at room temperature for slightly over a month showed a creamed

layer of about 40 per cent, but this layer was hardly distinguishable in density from the lower layer. There was no separation of oil on top. When the bottle was inclined there was no sticky residue left clinging to the bottle adjacent to the creamed material. This would seem to indicate that there was no tendency toward oil separation in the creamed material. No film appeared on top of the creamed layer in this sample. Although creaming occurred when oven-tested, the material was easily redispersable and no distinct creaming occurred when centrifuge-tested nor in the conclusive shelf test for stability. Also, no oil separated when tested by all three procedures. Thus, for practical purposes, this formula would seem to meet the requirements of stability as defined in the early part of this paper.

Acidity

The pH of this formula was observed to be 3.6. Since this is lower than the pH of the skin [average normal about 5.5(3)], a sample of the formula was adjusted with N/10 sodium hydroxide solution (2.0 cc. of N/10 sodium hydroxide solution per 100 cc. of emulsion) to a pH of 4.7 in order to bring it nearer to the acidity of the normal skin. However, the product thickened and became somewhat curdy. When tested for stability in the oven, the degree of creaming seemed to be about the same as that of the sample unaltered in pH. But, separation of oil on top indicated that the former was a less stable preparation. It was also found that 4.0 cc. of N/10 sodium hydroxide solution per 100 cc. of emulsion brought the pH from 3.6 to 5.95 and that 2 cc. of 0.5% ammonium hydroxide solution brought the pH from 3.6 to 8.0. However, the emulsion was not as stable, when adjusted to a higher pH with either sodium hydroxide or ammonium hydroxide volumetric solutions, as when unaltered.

Skin Test

Although none of the ingredients in this formula were known to cause dermal irritation, limited skin tests were performed in order to verify the absence of undesirable dermal effects which might be expected from the use of this preparation. The emulsion was applied to the inner surface of the forearm of five women, three men, and one two and one-half year old child twice daily for a period of two weeks. No reddening or other indications of irritation were observed.

Comparison With "Standard"

When compared to the product obtained from the formula of Clarke and Flack no marked difference in stability was noted. Samples aged upon a shelf for a month or more showed pronounced creaming in the Clarke and Flack product but little or none in the above preparation, but a comparable degree of creaming was observed in both preparations when tested by means of the accelerated procedures. Neither preparation exhibited oil separation. The viscosity of the product obtained from the Clarke and Flack formula was somewhat greater than that of the acid emulsion. Also, greater stickiness was noted when the former was rubbed upon the surface of the skin. The pH of the Clarke and Flack formula was found to be about 8.5, while that of the above formula was 3.6.

Summary and Conclusions

Emulsions prepared with Span 80 and Tween 60 and with Aerosol NS-8 and Aerosol NC-9 in conjunction with a number of emulsification assistants were not stable when aged for a month. However, a number of combinations produced smooth emulsions when first prepared. Temporary stability with little or no creaming and no oil separation lasted for a period of one to a few days with different combinations. Such findings would suggest the application of combinations of these agents in preparations where only such limited stability would be required.

The acid emulsion formula prepared with Emcol MS-16 in conjunction with the emulsification assistants methyl cellulose and propylene glycol exhibited satisfactory stability during a month of standing undisturbed at room temperature. No separation of oil and only negligible creaming occurred. The small degree of creaming was easily redispersed with shaking. The pH is below that of the skin but the small amount of alkali required to raise the pH would indicate little titratable acidity. Limited skin tests resulted in the observation of no irritation from this emulsion.

It would therefore seem that the formula given above should prove satisfactory as a stable acid emulsion for external application. The non-irritant character and the composition of this preparation would suggest its use as a baby lotion. With modifications it should also be adaptable to other dermatologic preparations of pharmaceutical interest.

Addendum

A sample of the acid emulsion preparation described in the latter portion of this paper has been aged at room temperature for a period of approximately one year. Creaming has occurred to no greater extent than that reported at the end of one month. No oil has separated. A few vigorous shakes of the bottle redispersed the creamed material to form a smooth preparation. After a year of aging the product thus appears to be as elegant a preparation as after one month.

Acknowledgment

Acknowledgment is gratefully given to Dr. Ivor Griffith and Dr. Austin A. Dodge for their assistance in connection with the above-described study, and to Professor Linwood F. Tice for his invaluable counsel.

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WATER ECOLOGY *

By Louis Gershenfeld **

THE topic assigned to me covers a vast subject. I am to consider fresh-water life as a whole rather than one class of living forms and I am to speak about the mutual relations between the different aquatic organisms in their respective environments. In view of the nature of the symposium at this meeting, I will confine myself to a consideration of the ecology of surface waters which constitute the largest source for public water supplies in our country. In presenting this subject I stress, of course, the sanitary interests. Furthermore, I do not limit myself solely to personal experiences but select freely the vast array of material which are the results of investigative studies or researches of others.

Microscopic Aquatic Organisms

The natural aquatic population of surface waters consists of types of organisms which morphologically and in their behavior are of low and high degree. All forms of plant and animal life (low and high) are represented. Their existence and the types found are influenced naturally by biological, chemical and physical factors. Yet with the latter and even with a specialization and diversification among them, they are still characteristically aquatic.

Among this population we find the Algae (green, blue-green, yellow-green, brown and red algae and diatoms); Fungi (lower bacteria) (cocci, bacilli and spirilla); Higher bacteria (including iron bacteria and sulfur bacteria); True fungi (including molds and yeasts); Protozoa (including sarcodina or rhizopoda, flagellata or mastigophora, ciliata or infusoria); Rotifera (closely related to the nematodes or roundworms); Crustaceae (including water fleas, cyclops and ostracods); Higher Crustaceans (including the cray fishes or "crawfish", water lice, sow bugs and scuds); Bryozoa or Moss Animals; and the Sponges or Porifera. Among a large array of miscellaneous organisms are to be found:

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Numerous wormlike structures found among the Platyhelminthes (flatworms), Nemathelminthes (roundworms), Trochelminthes (trocal worms), Annelida (segmented worms including earthworms and leeches) and the Gastrotricha (arrow worms, etc.); Mollusca (including mussels and snails); Arthropoda (including the Arachnida with the water spiders, mites and bears and the Insecta with the waterflies, waterbugs, dragonflies, waterbeetles and watermoths); Vertebrata (including the Pisces with the large number of species of fish which dominate the open waters and the Amphibia including the frogs and salamanders); the Hydrozoa and the Archiogomatae or higher plants (including the hornwort, water weeds, mosses, pondweed, the grass like Isoetes (and Phragmites).

Bacterial Flora in Natural Waters

Bacteria are perhaps the most numerous and the most widely distributed of living matter found in water. Inasmuch as they serve as sanitary indices for potable water and for man's welfare, it might be advisable to indicate briefly the kinds of bacteria found in water.

There are first the (a) natural or true water bacteria, those bacteria which are indigenous to water. Then we have the (b) soil and plant bacteria, organisms not normally inhabitants of or indigenous to water but which may find their way therein by being washed frequently into it during rains and blown into it by winds. The last group are sewage bacteria, normal inhabitants of the intestinal tract of man and animals, but here we may also find bacteria which may be pathogenic to man if ingested. It is apparent that in Nature there is very little virgin water, for pure natural water very quickly becomes contaminated with various foreign substances either from the atmosphere or soil. For convenience the three groups will be divided:

(a) *Natural Water Bacteria*

I Bacilli

(1) Fluorescent bacteria—gelatin liquefiers as *Pseudomonas fluorescens liquefaciens* and non-gelatin liquefiers as *Pseudomonas fluorescens non-liquefaciens.*

(2) Chromogens—including orange (*Chromobacterium aurescens*), red (*Chromobacterium prodigiosum* and *indicum*), yellow (*Chromobacterium ochraceum*) and violet forms (*Chromobacterium violaceum*).

(3) Non-chromogenic rods (mainly species of *Achromobacterium* as *A. liquefaciens;* also *Protaminobactes*).

II Cocci

(1) Chromogens—mainly yellow pigment forms, including *M. luteus, flavus* and *cinnabareus.*

(2) Non-chromogenic as *Micrococcus candicans.*

(3) Sarcinal—mainly *Sarcinal lutea.*

(b) *Soil and Plant Bacteria*

Most of the soil bacteria are aerobic spore-bearing rods resembling *B. subtilis* in morphology and include *B. megatherium, B. mycoides* and *B. vulgatus.* Species of *Aerobacter* as *A. aerogenes* which are found especially on grain and plants are aerobic, non-sporeforming rods. Species of *Nitrobacter* and *Nitrosomonas* and other soil and plant bacteria may be isolated by the use of special culturing methods.

(c) *Sewage Bacteria*

The typical sewage bacteria are species of *Proteus* and certain members of the genus *Clostridium* as *Cl. sporogenes.* The intestinal bacteria are species of *Escherichia, Clostridium* (as *Cl. welchii*) and *Streptococcus* (*Streptococcus fecalis*). Pathogens as *Eberthella typhosa,* species of *Salmonella* and *Shigella* and *Vibrio comma* may be present.

In an examination of the types of bacteria isolated from waters (lakes, streams, rivers), the vast majority (even as high as 90 or 95 per cent) will be found to be gram negative rods. The remainder are gram positive spore bearing rods and cocci, the former predominating. Most of the species are chromogens and their biochemical activity is poor.

Natural or Self Purification

From the above, it is apparent that all kinds of organisms are always present, but their kind and numbers vary with the season, temperature, density, viscosity, salinity, light, water movement, available food and oxygen supply and other environmental conditions. It may be a shifting and transient population subject to waves of fluctuations with dominant species appearing at different periods, but with the representation of the groups to which they belong remaining fairly uniform.

In terms of their descriptive mode of occurrence, nature and size, one hears of the *plankton,* referring to the assemblage of microscopic organisms which float free (so-called wanderers) in water and can be readily collected by the use of nets or other collecting devices. The free-floating plankton population of lakes is known as *limnoplankton,* that of rivers as *potamoplankton* and of streams as *rheoplankton.* The latter term is frequently used when referring to drifting life in all floating waters. The organic debris in river deposits made up of muds and pollutional sediments yields a bottom or *benthal* environment in which the microscopic population may be different from that in the flowing water, as decomposition proceeds in a manner which is at variance with the latter. This anaerobic decomposition is at times spoken of as benthal decomposition.

The natural purification of surface waters is a complex phenomenon in which so many variable elements and factors play a role. It is an interesting study as it concerns the mutual relations between living microscopic organisms in a specific environment. It is unfortunate that more attention has not been and is not being made to the natural content of bacterial plant and animal life in surface waters as yielding more valuable information concerning good quality water. Their presence or absence will serve as more useful living guideposts from which one can obtain direction as to the degree of pollution and in judging the sanitary characteristics of waters in which they are found as well as frequently indicating suitable methods to be practiced in removing objectionable conditions. There is an urgent need for the introduction of an ecological system which will give the normal habitat of various living microscopic forms and also note their behavior to varying conditions of pollution.

In the process of self-purification in waters, there is a very effective symbiotic relationship which we must recognize cannot function to its maximum or only slightly if it is interfered with too much or badly upset. It is not possible to discuss this in detail. Let us, however, consider just a few of the cycles concerned in the natural self-purification of water and how any extensive pollution may interfere or upset this process. Algae and certain plants use up carbon dioxide and liberate oxygen. Bacteria decompose organic substances either by aerobic or anaerobic digestion. Most of the water bacteria are aerobes, and this requires oxygen for their functioning. The capacity of water for absorbing oxygen from the atmosphere varies with

the temperature and pressure and other physical conditions. It is apparent then that the dissolved oxygen content of a water will serve as a useful parameter as to whether conditions are suitable for self-purification. When a natural body of water saturated with oxygen (needed for aerobic bacterial activity) becomes heavily polluted, there is an immediate lowering of the dissolved oxygen content. This is due to the dilution with the polluted matter which is either poor or deficient in dissolved oxygen, and secondly to a gradual depletion in oxygen by the bacteria and other organisms due to their increased activity in the decomposition of the organic waste matter. Dissolved oxygen is urgently needed in nature's scheme of self-purification but with excessive pollution the dissolved oxygen content becomes depleted and nature is unable fully to carry out her work of purification.

The demand placed upon oxygen resources by the natural digestion of organic matter has resulted in the introduction of the B. O. D. (Biochemical Oxygen Demand) test. B. O. D. determinations can serve a useful purpose within certain limitations, but one must recognize these limitations. For instance it has been noted by various workers that in a year of low water, the B. O. D. changes with the degree of sewage destruction. On the other hand, the average B. O. D. is usually lower in a year of high water due presumably to a greater dilution. It is not any pollution which may have been introduced but the condition of the river as affected by its stage which accounts for the findings. Again one may find that B. O. D. safe limits as noted in some regulations are too arbitrary. This is well pointed out in instances where waters containing inhibiting agents (as acids, iron compounds and other chemicals which are trade wastes are polluting such waters) will give values far under that fixed by regulatory action as a safe limit. One must be sure that in interpreting B. O. D. findings, they are considered as in the case of other laboratory findings with factors such as a history of the sample, report of field survey, etc.

Many of the bacteria found naturally in water aid in maintaining the world's food supply but are also of value in self-purification. Let us consider the nitrogen cycle. The presence of species of nitrate- and nitrite-forming organisms in water is in great measure responsible for the various forms of nitrogen and the latter are, of course, subject to quantitative change. Some of these nitrogenous substances are needed for the food of aquatic life and their absence or presence may produce a change in the flora or fauna.

It is readily apparent how extensive pollution may interfere with the nitrogen cycle. Let us, however, remember that even high findings must be properly evaluated.

We are all familiar with the significance of high ammonia content as signifying recent pollution and its value as a warning sign if traced to that of animal origin. Here, too, we must consider the source and recognize that mineral sources and trade wastes may increase these values. Even high nitrate findings may not mean considerable danger unless the values of other forms of nitrogen and organic matter are low.

The decomposition of nitrogenous substances by biological agencies with the production of ammonia is known as "ammonification". Numerous bacteria and soil fungi play a prominent part in this process. From the agricultural standpoint, the process of ammonification is one which assists in making available food for plants. Ammonia and its compounds are not assimilated to any extent by plants, but as soon as these are produced, they are changed into nitrates. This, a process of oxidation, and known as "nitrification," is brought about by bacterial activities and accomplished in two steps. The ammonia compounds are oxidized or transformed first into nitrites and then into nitrates.

The nitrite-forming bacteria are members of the genus *Nitrosomonas*. The nitrate-forming bacteria are at present grouped in the genus *Nitrobacter*. These nitrifying organisms occupy a unique position in relation to the bacterial kingdom and the higher forms of plant life. They are capable of growing and developing upon inorganic material solely. Though they do not possess chlorophyll, they seem capable of utilizing atmospheric carbon dioxide without the aid of sunlight, which they probably use for their carbon supply.

Sanitary Analyses and Sanitation

Sanitary analyses have been carried out and designed mainly to supply information as to the wholesomeness of water and as to its accepted fitness for general domestic use. The choice of tests most suitable may vary for different waters. In all instances, however, a bacteriological examination is usually conducted. Everyone is conscious that the chief danger associated with water is the possible conveyance to those who drink it of the causative agents of typhoid and paratyphoid fevers, dysentery, cholera and other intestinal

diseases. These pathogens are responsible for the so-called water-borne diseases. It is the latter more so than anything else which have been responsible for our interest in the water we consume and for most of the progress in water sanitation. Human sewage (untreated or inadequately treated) polluting water supplies is in great measure responsible for these water-borne diseases.

It is important to point out that the very impressive decline in the incidence and fatality rate of typhoid fever in Europe and North America during the last 75 years may have created in the minds of everyone, layman and health workers alike, the impression that this and even other water-borne diseases have been eradicated. Laxity in control measures has occurred and is occurring in some areas.

In many small communities the control over the safety of water supplies is inadequate.

The public health hazard is significant and the resultant potentially dangerous conditions are not only disconcerting but serious.

It is believed that the causative agent of infectious (epidemic) hepatitis is transmitted by water infected with the virus from the feces of diseased individuals. Present methods of water purification (chlorine disinfection, etc.) appear to be inadequate and a water free of fresh or recently discharged sewage is the only answer. May I point out here that this is the first water-borne human virus disease definitely traced to infected water. One wonders about the relationship between other virus diseases and infected water. In this connection, nothing was mentioned above in the general ecological consideration concerning the presence in water of pathogenic viruses and bacteriophage, for our knowledge concerning their significance in water is meagre. I am not considering bilharzial and other animal parasitic infections, for in this area we fortunately are not at present concerned with them.

In the state of Pennsylvania, there is an estimated total of 100,000 miles of streams, one-quarter of which are virtually in their natural state of purity. An additional approximate forty per cent of the total is comparatively clean water, fit for use for water supply with proper treatment and suitable for recreational purposes and for fishing. The remaining 35,000 miles of stream waters are heavily polluted by acid coal mine drainage and at present unfit for general use.

The basic rule of the common law is that each riparian proprietor has the right to have water in a pond, stream or river come

down to him with its quality unimpaired and with its quantity undiminished except in such manner and to such extent as may result from its reasonable use by riparian proprietors above him.

The latter may use the water for natural purposes but then cannot wantonly or recklessly contaminate or befoul the water. Discharging waste from a mine or a manufacturing plant or dumping raw sewage into a stream is not a natural use of the stream. Furthermore it causes material injury to the lower riparian proprietors. Even if the manufacturing plant benefits the public, this is no excuse for polluting the water.

Pollution in most instances is caused by the discharge of sewage untreated or partially treated from public and private cesspools, septic tanks, garbage dumps and industrial wastes. The problem in Pennsylvania is primarily one of untreated sewage and of industrial wastes. There are the deposits of culm waste from coal mining operations, spent pickle liquors from the steel and allied plants, trade wastes from tanneries, chemical, textile, synthetic rubber and allied plants, from oil production and refining, other mining wastes and even from milk processing.

The results of pollution are manifold. The quality of water for community use leaves much to be desired; for even though the water is rendered safe, there may be some objectionable physical quality as a clouded and colored water or one possessing an odor and taste. The recreational uses of polluted streams are frequently destroyed so that fishing, boating, swimming and even picnicking on the banks may be impossible. The damage to water-front property and soil erosion are factors to be considered. Objectionable odors prevent the use of polluted waters for navigation; and workers engaged in industries found in buildings along the banks complain of the nauseating effects of such odors. These are only a few of the results which follow the lack of a clean water. I have not even considered such factors as the preservation of natural aquatic life and keeping Nature's stream really a beautiful sight to behold.

Conclusion

In concluding this presentation, let us recognize that stream pollution in Pennsylvania and elsewhere in this country has been growing, and growing very rapidly, for more than a century. There has been too much talking during the last 25 years and com-

paratively little action. We know what causes the condition. We must therefore treat the cause wherever possible at its source and avoid taking chances with polluting our streams. There must be adequate treatment of sewage and better controls practiced over the discharge of all industrial wastes causing water treatment difficulties. Mines should be sealed. Better control at the source will mean that our streams will not be heavily polluted. Nature's living aquatic forms will then do their share to give us a water suitable for all purposes and adequate for making available with but little treatment a high quality palatable water, clear and colorless, non-corrosive and free from pathogens.

We must recognize that this task of stream improvement must be well coordinated. The time is now at hand inasmuch as the war is over. Individual and special interests must give way to community interests. Regional Boards working with and under the jurisdiction of a central State-wide controlling Board which in turn cooperates with a central national controlling Board, all being functioning Boards, may evolve a procedure of action satisfactory to the majority.

The science of public health is far in advance of the art of its practical application. Too many frequently accept the past achievements in this field as finished accomplishments. This result is the development of a false sense of security, when actually the victory is far from complete; and it is this which should serve as a constant challenge to professional and public health workers to be ever watchful in any attempt to finish the task effectively.

IT'S ALL IN THE MIND!

By T. Swann Harding

WELL, well: "Sell By Smell" is the latest advertising slogan. A recent experiment, using the public as guinea pigs, showed what could be done. Consumers were shown identical pairs of hosiery —one almost unnoticeably scented, the other not scented at all. They bought the scented hose by preference because, they said, it had better texture and more appealing color! Fastidious stenographers found out that scented carbon paper smudged less than the identical product unscented! Women are partial to handbags with the robust masculine scent of wild fern on them. It's all in the mind!

It reminds me of the people who have been telling me all my life that reading on moving vehicles or in poor light would ruin my eyes. I did and it simply didn't. Carefully controlled tests by scientists back up my experiment too. They provide no concrete evidence whatever that reading while in motion or in poor light injures the eyes any more than it would injure the nose to smell weak scents on a bus (which, alas you don't). It's all in the mind!

Dim light no more injures the eyes than slight odors injure the nose or faint, indistinct sounds the ears. Poor illumination does not cause nearsightedness, nor is this condition the result of close work on glossy paper in poor illumination. There is no ground either for the assumptions that light should come over the left shoulder or that reading on trains or in bed ruins eyesight. Eye fatigue is usually fatigue of attention, and it produces psychological disturbances rather than organic eye diseases.

True, medical publications have accepted and enshrouded many pseudoscientific beliefs regarding illumination and the eyes, just as they have regarding rackets and the ears. Glasses do not necessarily preserve and incorrect lenses damage the sight. Nor does work under artificial light *per se* strain the eyes. So say qualified oculists.

But there is no limit to what the human mind can conjure up in this field. A while back Western Electric found out that its workers increased production when better illumination was afforded them. But it also discovered that when a mock change was made in light intensity, and the illumination afforded was rendered poorer, the workers

increased production just as much. In other words any change is helpful, *if recommended as beneficial.*

As illumination increased, workers expressed greater satisfaction. But when at last the old bulbs were removed and new ones of exactly the same kind were inserted, the workers still expressed increased satisfaction! As illumination was decreased, the same thing occurred. A point was reached where the workers began to say that the lights were too dim and they found them increasingly dim even after a mock change was made. The same general things were true of ventilation, temperature, humidity, and other factors.

Hence the effects of our physical surroundings are more "psychological" than "real," though real enough insofar as they affect us. Our complaints about our surroundings are always admixtures of fact and fancy, never statements of fact, in which our relations with our families, our bosses, and our fellow-workers are inextricably comingled. We say a room is hot (or cold), a tool is dull, a machine is out of order, the ventilation is bad.

But what do these statements really mean? They may mean that our physical condition is poor, that we had a spat with our wife or husband or supervisor, that we feel frustrated, or that our broad social status at work is wholly unsatisfactory. Changes of physical circumstances are never clearly, directly, and significantly responsible alone for variability in our behavior or our output rate. So much is in the mind. So little of the effect is in the eye or illumination *per se.*

Quite similarly people have been saying for years that there are unearthly screeches which will kill a person yards away and that constant exposure to loud noise impairs hearing, while temporary exposure to very loud noise does the same. Yet, during the late unpleasantness, the gay and kindly scientists sought to find the lethal sound bolt so as to smite our enemies by land and sea. All sorts of magical noises were tried, and found wanting. In fact nothing was found, except that all sounds in the neighborhood of 120 decibels in intensity are very odious.

Of course ominous sounds are different. If the mind invests the sound with horror it can unnerve the individual or unhinge the mind. But here again the injury depends on what we think the sound means, not on the sound itself.

It is true also that extremely loud blasts can burst the eardrums and that constant very loud noise has a temporary ill-effect on hear-

ing, but the latter does no permanent damage. The ear quickly regains its sensitivity and working in a noisy place does not impair hearing. In fact the work efficiency of docile people who imagine they have to have quiet to be proficient is not at all impaired if they work while exposed to loud noise. So how do you account for that?

So it goes right up and down the line. No wonder psychosomatic and psychoneurotic conditions accounted for 80 per cent of all ills of our armed forces. Emotional factors have a great deal to do not only with individual resistance to germs and viruses, but also with the development of asthma, hay fever, gastric ulcer, high blood pressure, and coronary disease. Take a thing like insomnia. You can get along exceedingly well with very little sleep, provided you don't worry about not sleeping.

But not long ago a distracted, dishevelled man came in anguish to a doctor in what is perhaps our best known clinic. He was a victim of chronic insomnia. He had seriously decided to take his own life if he didn't recover. A friend suggested this famous physician as a last resort and, with no faith in him at all, the man came. But the doctor listened to him less than five minutes then, talking as he took several books down from his shelves, he said:

"I'm awfully sorry, but I just haven't the time to take your full history and prescribe for you this afternoon. It's terribly unfortunate, but I have to attend a wedding and a wedding reception and tonight I must give a talk at a clinic. But I'll see you first thing in the morning. I'll even get into the office at eight so you won't have to wait. Meanwhile suppose you take these books along to read while you are awake tonight. You'll find them interesting and there are enough to last the night through, I'm sure."

At ten the next morning the patient slunk sheepishly in. The doctor, who handn't expected him until eleven, looked up and the patient said:

"I'm sorry, doc. But I went to sleep over those damned books at nine o'clock last night and I never woke up until half an hour ago. I came right on down without my breakfast." That cured the insomnia. He never suffered again. But explain it. Why?

The doctor couldn't explain it to me. Instead he told me a story on himself. He tells this story to too credulous research students as a warning. He had an attractive female patient with red hair, who was ill at her home. The family wanted a nurse for her. So he took

one over, attractive, competent, but also red-headed. Soon a member of the family gave him the high sign for a private conference and they went off into another room where this woman, the patient's mother, said:

"She's lovely, doctor, but she would never do. She has red hair. So has my daughter. Two red-headed people can never get along, you know that. They never have. They never will." The doctor thought that very silly, but he didn't say so. Instead he remarked:

"I'm sorry, but it's that nurse or no nurse. You know what the nursing situation is today. Shall I take her to another patient? I have five who would be glad to have her and she's all I can get."

She remained. She and the patient got along famously. The doctor congratulated himself on having used scientific method to explode a superstition. But one day two weeks later he happened to observe something. The nurse had been unable to get a hairdresser and now a little black hair was distinctly growing up from the roots. She saw him looking.

"Don't shoot, doc," she said. "I'll confess. I'm not a redhead. That's all a fake. My hair's almost black." How do you explain it?

Many people tell me that they recognize the brands of cigarettes they smoke. Yet those expert in cigarette manufacture say that all brands at about the same price are equally good and practically indistinguishable. If you mix unidentified cigarettes together they all seem to please. If smokers are blindfolded in controlled tests they fail utterly to identify their favorite brands or to pick out those to which they have an aversion. Is it all in the mind, in the sight, or in the nose?

It is possible to remove the characteristic color from chocolate without changing its flavor or nutritive value. If two lots of candy are now made, one with the unaltered and one with decolorized chocolate, subjects of test will invariably describe the latter as tallowy or otherwise objectionable in taste. Blindfold the subjects, however, and they can't tell the difference between the two! Either the nose knows or the mind is whimsical or we believe only what we see. Remember those scented hose!

Many experiments have been performed to determine whether coffee keeps people awake at night. I have run some of them myself. For a great many people can drink decaffeinized coffee with impunity. However, if I can slip some unaltered coffee over on them while mak-

ing them believe it is decaffeinized, they can drink even two or three cups of it and sleep well. Scientists perform this sort of experiment more carefully.

For instance, they will give the same subjects coffee one night and milk the next, at the same hour. All of them go to sleep faster after drinking the milk, too—provided they are not told that the milk is spiked with three times as much caffeine as the coffee contained, and that must prove something. If they knew that the milk was spiked it, also, would undoubtedly keep them awake. So it seems the only obvious thing to do to defeat the mind's efforts to befuddle us is to experiment with people customarily assumed to have no minds, the insane.

That also has been done. Just before the war an English physician who acted as consultant at a mental institution observed that the insane, like the sane, could not "function well" unless they regularly took cathartics or laxatives. His mentally deranged patients regularly demanded their white powders. He could not take this medicine away from them as that would have been cruel. They clung to it as the last stable feature of an otherwise unruly and tempestuous world.

So the doctor began very gradually to substitute a white substance which had no laxative power at all for the chemicals ordinarily composing the beloved white powders. Ultimately he had made a complete substitution. No original ingredient was present and the patients were taking a mere non-laxative powder. However, they "functioned" just as well as on the white powders and manifested satisfaction.

That this same system works on the supposedly sane has been proved by many manufacturers of patent or proprietary remedies. Over and over again war and other emergencies over which they had no control deprived them of the sovereign ingredients for their remedies. They therefore changed formulas, sometimes completely, but kept the old label name and claims. Provided alcohol, if originally present, was retained at normal strength, the remedies worked quite as well as ever when composed of wholly new ingredients.

This was not so phenomenal when it is remembered that many of these remedies had worked potently for years while containing no ingredient except alcohol that was known to have any physiological effect. Wholly voluntary, unsolicited, nonpay testimonials proved

these things. This indicates that bottled psychotherapy also makes a powerful drug.

Then take me. I am convinced that one certain brushless shaving cream is superior to all others. Druggists assure me this is untrue. Chemists inform me that the formula is identical with that of two other brushless creams, both of which I find atrocious. I tell you it's all in the mind, whatever little there is of it.

SELECTED ABSTRACTS

Stability of Crystalline Sodium Penicillin. G. B. Berk, B. M. Shepard and C. Glaser. *Science 105,* 239 (1947). It was noted that solutions of crystalline preparations of penicillin G (5,000 units/ml.) exhibited lower stability when stored at either 15° or 24° than earlier, cruder preparations. This behavior was considered to be due to the removal during the purification process of impurities which acted as buffers.

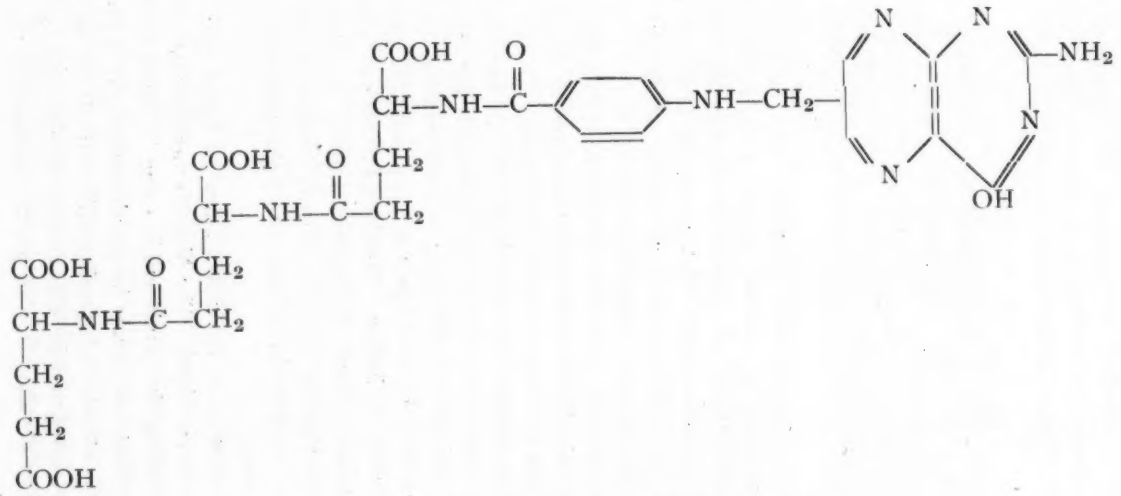
Studies made on solutions of crystalline penicillin (5,000 units/ml.) buffered with sodium bicarbonate, acetate, succinate or citrate in a concentration of about 5 per cent by weight of the penicillin present indicated that stability was maintained for at least 7 days at 15° and 4 days at 24°.

The average loss of potency for solutions of 10 batches of penicillin buffered with sodium citrate and stored at 15° for 7 days was only 1 per cent, whereas unbuffered controls lost an average of 26 per cent under the same conditions.

The authors conclude that the decomposition of sodium penicillin in solution appears to be autocatalytic, and that the rate of inactivation increases rapidly as the temperature rises.

Synthetic Folic Acid: The Effectiveness of a Conjugated Form in the Treatment of Tropical Sprue, Addisonian Pernicious Anemia and Nutritional Macrocytic Anemia. T. D. Spies, G. G. Lopez, F. Milanes and T. Aramburu. *J. A. M. A. 134,* 18 (1947). Folic acid, which is a member of the vitamin B complex, occurs in nature in the free form and also as a part of various complexes. The authors report the treatment of one case each of sprue, addisonian pernicious anemia and nutritional macrocytic anemia by the administration of synthetic pteroyldiglutamyl-glutamic acid. This substance differs from folic acid (*Lactobacillus casei* factor) in that it contains two more molecules of glutamic acid; it is not excreted so rapidly in the urine of patients with macrocytic anemia as is the *L. casei* factor.

The authors present a detailed report of the case of tropical sprue treated with the synthetic drug, which was administered intra-



Pteroyldiglutamyl-glutamic acid.

muscularly in a daily dose of 10 mg. for 8 days. A marked hematologic and clinical response was observed. Similar results are stated to have been obtained in the other two cases.

Numerous investigators have noted that a large amount of folic acid or related compounds is necessary to produce a satisfactory hemopoietic response, in contrast to a relatively small amount of the active substance from a potent extract of liver.

The Clinical Use of Anticoagulants. Report of Treatment with Dicumarol in 1,686 Postoperative Cases. E. V. Allen. *J. A. M. A. 134,* 323 (1947). This paper constitutes the Chairman's Address in a symposium on "Treatment," held by the Section of Experimental Medicine and Therapeutics at the 95th Annual Session of the A. M. A.

The author urges that more attention must be given to the desirability of impairing the clotting power of the blood within blood vessels. Far more deaths are caused by intravascular coagulation of the blood than by hemorrhage. Reviewing the literature on heparin and Dicumarol, he finds that these are fairly satisfactory anticoagulants, although they possess certain deficiencies.

The author and his associates administered Dicumarol in 1,686 postoperative cases. Minor hemorrhage occurred in 3.1 per cent and major hemorrhage in 1.9 per cent of these cases. Of two deaths resulting from hemorrhage, one was definitely not attributable to the drug, and there was doubt that it was responsible for the other.

Dicumarol was used in 280 cases of postoperative venous thrombosis, 716 cases of abdominal hysterectomy, and 292 cases of postoperative pulmonary embolism. Based upon clinical experience in such cases handled without the administration of Dicumarol, the author believes that proper use of this drug resulted in the saving of 73 lives and that venous thrombosis and pulmonary embolism were averted in 211 cases.

The administration of Dicumarol must be based upon the value for prothrombin in the blood. The Magath modification of the Quick method for calculating the prothrombin value is stated to be reliable. With this method normal values for prothrombin give a prothrombin time of 19 to 21 seconds. A prothrombin time of 27 seconds indicates 30 per cent prothrombin; 35 seconds, 20 per cent; 60 seconds, 10 per cent. These values are of great assistance in the adequate

dosage of Dicumarol, for clinical experience has demonstrated that intravascular thrombosis rarely occurs when the percentage prothrombin in the blood is less than 30, and bleeding rarely occurs when the percentage is 10 or more.

The customary dosage of Dicumarol is stated to be 300 mg. on the first day, and 200 mg. on the second day. Subsequent dosage is based upon the percentage prothrombin found on examination of the blood.

If excessive hypoprothrombinemia is induced by the administration of Dicumarol, the condition may be corrected by giving 30 to 60 mg. of a synthetic vitamin K preparation intravenously, repeated at 4 to 6 hour intervals 2 to 3 times as necessary. Transfusion of 500 cc. of blood may also be given if the hemorrhage is severe.

The respective merits of the ligation of veins and the administration of anticoagulants are also discussed.

Antiseptic Action of Glycerite of Hydrogen Peroxide on *Mycobacterium tuberculosis* (var. *hominis*). E. A. Brown and L. W. Slanetz. *Science 105,* 312 (1947). The hydrogen peroxide preparation used in this study contained 1.5 per cent of the compound as derived from urea peroxide (4 per cent) dissolved in anhydrous glycerol, with 0.1 per cent of 8-hydroxyquinoline as a stabilizing agent.

Bactericidal action against *Mycobacterium tuberculosis* (var. *hominis*) *in vitro* was observed when the glycerite of hydrogen peroxide had a concentration of 0.5, 1, 2 and 4 per cent (given as total urea peroxide). The tests were conducted by pipetting 0.1 ml. of the solution to be tested into porcelain penicylinders placed centrally on Petri dishes containing an agar culture averaging 9,000,000 organisms per plate. After incubation of the plates at 37° for 3 days the zones of inhibition were measured. No viable organisms could be demonstrated by subculture technique in which samples of agar from the clear zones were tested.

Bacteriostatic action was demonstrated for phenol 2, 3, 4 and 5 per cent; sulfaguanidine 1 per cent; sulfadiazine 5 per cent; and sulfamethazine 10 per cent. Penicillin exhibited no measurable effect.

Other *in vitro* experiments indicated that a glycerite containing 8 per cent hydrogen peroxide (total urea peroxide) is probably bactericidal for *Myco. tuberculosis* in periods of about 2 hours and with certainty in periods of more than 1 but less than 24 hours.

Clinical studies were performed by J. Goldberg on four patients with abscesses which were positive by smear and culture for *Myco. tuberculosis.* The glycerite of hydrogen peroxide (urea peroxide 4 per cent) was applied as a wet dressing two to six times daily. No other treatment was used, and all previous treatment had been ineffective. In three patients, the abscesses healed completely within periods ranging from 4 to 11 months. The fourth patient improved considerably but was still under treatment when the clinical report was made, which was a year after the conclusion of treatment on the last of the three healed cases. It was thus demonstrated that the healing did not constitute merely a temporary remission.

Tridione in the Treatment of Epilepsy. W. G. Lennox. *J. A. M. A. 134,* 138 (1947). Tridione, which is 3,5,5-trimethyloxazolidine-2,4-dione, was administered to 166 patients having a petit mal type of seizure. This term includes petit mal (or pyknoepilepsy), with transient but frequent lapses of consciousness; second, myoclonic jerks; and third, akinetic (loss of posture) seizures. In this series, 83 per cent of the cases showed improvement and 31 per cent became entirely free of seizures; 13 per cent were unchanged; and 4 per cent experienced an increase in the number of attacks.

In contrast, the author's clinical observations on the use of the drug in psychomotor or grand mal seizures do not support claims that Tridione is an anticonvulsant. Of 58 patients having frequent grand mal seizures (with or without complicating petit mal), 21 per cent had less frequent and 50 per cent had more frequent convulsions. In an additional group of 35 patients having psychomotor seizures, Tridione when used alone was ineffective. In a few cases, however, a combination of the drug and diphenylhydantoin sodium appeared to be of some benefit.

Toxic reactions to the drug included photophobia in 31 per cent of all cases treated, rash in 14 per cent, and various other manifestations with lesser frequency. The author cautions against a possible toxic effect on the bone marrow, advising monthly blood examinations and discontinuance of medication if neutrophils fall below 1,600 per cu. mm.

Preliminary trial of an experimental homologue, dimethylethyloxazolidine dione, indicated that it was somewhat more effective in petit mal than Tridione and also less toxic.

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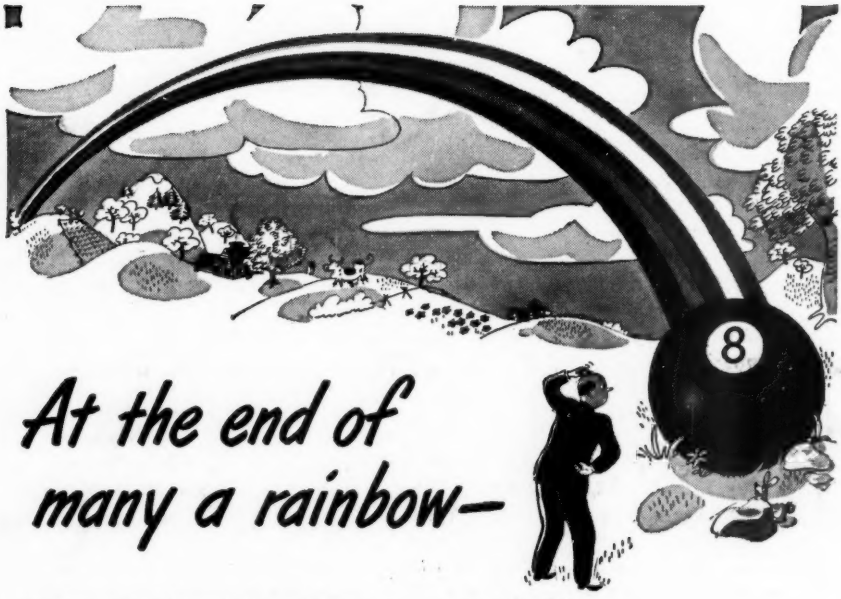

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